



# Shaping the future of health care to prevent, control, and cure diseases.

# **History/Evolution**

Cancer exerts a phenomenal toll on the American public. It is estimated that 563,700 Americans will die of cancer in 2004, 9.6 million (M) Americans alive today have a history of cancer, and 1.368M Americans will be newly diagnosed with the disease this same year. In the past decade, heightened public awareness and increased interest in health issues have influenced scientific research. Cancer research has drawn particular attention, due in part to the rising impact of cancer and the work of highly visible consumer advocacy organizations. (See the related box story on page I-6 about how consumer advocacy has impacted science policy.)

In response to these concerns, the U.S. Congress directed the Department of Defense (DOD) to manage intramural and extramural research programs that focus on specific diseases. The U.S. Army Medical Research and Materiel Command (USAMRMC)<sup>2</sup> has been responsible for managing targeted appropriations totaling almost \$3 billion (B) for fiscal years 1992–2004 (FY92–04) for research on breast, prostate, and ovarian cancers; neurofibromatosis; peer reviewed medical research; chronic myelogenous leukemia; tuberous sclerosis complex; myeloproliferative disorders; and other health concerns. Together, these programs comprise the Office of the Congressionally Directed Medical Research Programs (CDMRP), a scientific research directorate within the USAMRMC.

After the U.S. Army received the initial \$210M appropriation for breast cancer research, the Army sought the advice of the National Academy of Sciences (NAS) to effectively manage the funds. In response, the NAS Institute of Medicine (IOM) issued a report entitled Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command. The IOM committee made several major recommendations in this report. First, the committee recommended an annual investment strategy to guide allocations of

recommended an annual investment strategy to guide allocations or funds that best address the current needs in breast cancer research. Second, the committee recommended a two-tier

review strategy consisting of scientific peer review and programmatic review. This two-tier review system was designed to ensure that the research portfolio reflects not only the most meritorious science but also the most programmatically relevant. Both of these recommendations have become cornerstones in the administration of most of the programs managed by the CDMRP. Further descriptions of the annual investment strategy and two-tier review process can be found in this section under Program Execution and Science Management.

<sup>1</sup> American Cancer Society - Cancer Facts and Figures, 2004.

<sup>&</sup>lt;sup>2</sup> Known as the U.S. Army Medical Research and Development Command prior to 1995.

# **Programs Managed by the CDMRP**

The CDMRP is enabling the nation to cure diseases. Since its inception, the CDMRP has managed 40 separate research programs that are aimed at improving the health of all Americans. Congressional appropriations directed toward these 40 research programs total almost \$3B.

Eight of the programs managed by the CDMRP are considered core programs. Core programs have either received or have the potential to receive multiple appropriations and are characterized by standing Integration Panels (IPs) composed of expert scientists,

clinicians, and consumer advocates. The other programs managed by the CDMRP are characterized by a one-time appropriation and/or are institutionally based programs. Although the programs within the CDMRP share many common features, each program is unique and emphasizes the specific needs of its research and advocacy communities. Highlights of each of the eight core programs follow with additional details found in the corresponding program sections. Additionally, Section XI of this report contains information on the other programs managed by the CDMRP.

## Breast Cancer Research Program

The DOD Breast Cancer Research Program's (BCRP's) vision is to eradicate breast cancer. The BCRP has managed approximately \$1.67B in appropriations from FY92 to FY04 and is the second largest funder of extramural breast cancer research in the world. The program is also a recognized leader in innovative program management. In an effort to accelerate medical discovery and eradication of breast cancer, a research portfolio has been built that encompasses a wide spectrum of projects spanning the prevention, detection,

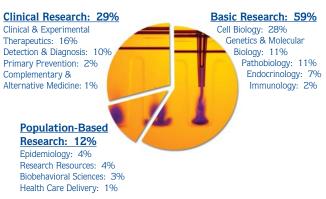


Figure I-1. FY92-03 BCRP Portfolio by Research Area

diagnosis, and treatment of breast cancer (Figure I-1). Awards made through this program support innovative ideas, the training of future generations of scientists and clinicians, necessary research resources, and translational research. Through FY03, the BCRP has received over 22,600 proposals and has made 4,073 awards. The BCRP is described in greater detail in Section III.

# Prostate Cancer Research Program

The DOD Prostate Cancer Research Program's (PCRP's) vision is to conquer prostate cancer. As a leader in support of prostate cancer research, the PCRP has been responsible for the management of \$565M in appropriations through FY04. The program has supported basic, clinical, and population-based research directed toward eliminating this life-threatening disease (Figure I-2). In addition, the PCRP is committed to addressing the significant disparities in the incidence and mortality of prostate cancer that exist among different

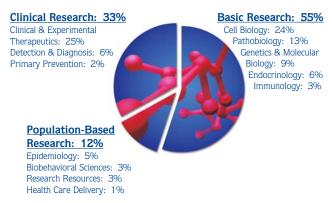


Figure I-2. FY97-03 PCRP Portfolio by Research Area

ethnic groups, and it has designed several award mechanisms to stimulate research in this area. Through September 2004, more than 4,200 proposals have been received, leading to 1,013 awards. Additional details regarding the PCRP are included in Section IV.

# Neurofibromatosis Research Program

The DOD Neurofibromatosis Research Program's (NFRP's) vision is to decrease the impact of neurofibromatosis (NF) and schwannomatosis. As a leader in NF research funding worldwide, the NFRP has managed \$130.3M in congressional appropriations from FY96 to FY04. The NFRP has supported a multidisciplinary portfolio aimed at improving and enhancing quality of life of persons with NF and schwannomatosis (Figure I-3). In recent years, the program has placed emphasis on funding ground-

Basic Research: 72% Cell Biology: 49% Genetics & Molecular Clinical Research: 9% Biology: 21% Clinical & Experimental Endocrinology: 1% Therapeutics: 8% Pathobiology: 1% Detection & Diagnosis: 1% Population-Based Research: 19% Research Resources: 13% Biobehavioral Sciences: 2.5% Epidemiology: 2.5% Health Care Delivery: 1%

Figure I-3. FY96–03 NFRP Portfolio by Research Area

breaking ideas and bringing laboratory research to the clinic. The clinical emphasis of the program includes the support for large natural history studies/consortium awards, the development and evaluation of preclinical model systems, and clinical trials. From FY96 to FY03, the NFRP received 362 proposals that have led to 117 awards. Further details on the NFRP appear in Section V.

# Ovarian Cancer Research Program

The DOD Ovarian Cancer Research Program's (OCRP's) vision is to eliminate ovarian cancer. The OCRP has built a multidisciplinary portfolio (Figure I-4) that spans basic, clinical, and population-based research as well as research resources. Over the years, the program has offered awards to invigorate the field of ovarian cancer research through the support of collaborations across disciplines and institutions, funding for pioneering research, and the training of new investigators in the ovarian cancer field. Appropriations for



Figure I-4. FY97–03 OCRP Portfolio by Research Area

the FY97–04 OCRP total \$81.7M. Since the program's inception through FY04, 710 proposals have been received and 80 awards have been made. The OCRP is described in greater detail in Section VI.

# Peer Reviewed Medical Research Program

The DOD Peer Reviewed Medical Research Program's (PRMRP's) mission is to support research on issues with direct relevance to military health. Appropriations for the FY99–04 PRMRP total \$244.5M. In the first 5 years of the program, the PRMRP has developed a portfolio of research that covers 127 medical research projects in 45 topic areas that have direct relevance to military health. Figure I-5 reflects the FY99–03 portfolio by research area. An important feature in the execution of



Figure I-5. FY99-03 PRMRP Portfolio by Research Area

this program is the use of an advisory panel composed of representatives from the Army, Navy, Air Force, Marines, Department of Veterans Affairs, Office of the Assistant Secretary of Defense (Health Affairs), and U.S. Department of Health and Human Services to develop an investment strategy and conduct programmatic review. Additional features of the PRMRP are detailed in Section VII.

# Chronic Myelogenous Leukemia Research Program

The DOD Chronic Myelogenous Leukemia Research Program's (CMLRP's) vision is to perfect the existing treatments and develop new diagnostic and therapeutic approaches for chronic myelogenous leukemia (CML). The CMLRP was established in FYO2 and to date the program has managed \$13.5M in congressional appropriations for research

Clinical Research: 32%
Clinical & Experimental
Therapeutics: 28%
Detection & Diagnosis: 4%

Basic Research: 68%
Cell Biology: 25%
Genetics & Molecular
Biology: 18%
Research Resources: 11%
Immunology: 7%
Pathobiology: 7%

Figure I-6. FY02-03 CMLRP Portfolio by Research Area

in CML. A total of 28 awards have been made through FYO3 to improve the understanding, diagnosis, and treatment of CML and enhancement of the quality of life of persons with the disease. The projects funded by this newly established program encompass both basic and clinical research (Figure I-6). The CMLRP is described in more detail in Section VIII.

# Tuberous Sclerosis Complex Research Program

The DOD Tuberous Sclerosis Complex Research Program's (TSCRP's) vision is to lessen the impact of tuberous sclerosis. The TSCRP was established by a \$1M appropriation in FYO2 for tuberous sclerosis research, and to date the program has managed \$6M in congressional appropriations. The TSCRP has funded seven awards through FYO3 aimed at elucidating the role and function of proteins produced by the *TSC1* and *TSC2* tumor suppressor genes. More detailed information regarding the TSCRP can be found in Section IX.

# Myeloproliferative Disorders Research Program

The DOD Myeloproliferative Disorders Research Program's (MPDRP's) mission is to support research on three chronic myeloproliferative disorders including polycythemia veva, idiopathic myelofibrosis, and essential thrombocytosis with direct relevance to military health. The program was established in FYO4 by a \$4.25M appropriation. Further information on the MPDRP appears in Section X.

# Program Execution and Science Management

An important feature of the CDMRP is its ability to adapt to the current needs of the research, clinical, and consumer communities. The CDMRP utilizes a flexible 7 year execution and management cycle that spans all phases of program execution, from the development of a vision through the completion of research grants (Figure I-7). All programs within the CDMRP depend upon yearly, individual congressional appropriations. These funds are not in the President's budget; Congress adds them annually to the DOD appropriation to fund new programs or to augment existing DOD or Army programs. The effectiveness of the programs, the work of consumer advocates, and

the need for additional, focused biomedical research have led to continuing appropriations for programs managed by the CDMRP.

# **Early Program Planning**

Early in each FY, after the congressional appropriation has been signed into law and funds have been received by the USAMRMC, each program's IP—an expert panel of scientists, clinicians, and consumer advocates—meets to deliberate issues and concerns unique to the individual program and establish a vision and investment strategy for the coming year. The development of an annual investment strategy stems from the 1993 IOM recommendations<sup>3</sup> and provides a high degree of flexibility. It allows each

<sup>&</sup>lt;sup>3</sup> Institute of Medicine, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, 1993.

# Fran Visco: "An activist for breast cancer research. Her ally: The U.S. Army."

Adapted from "In the vanguard" by Marie McCullough, Philadelphia Inquirer July 5, 2004.

"In the vanguard" is the story of how one breast cancer survivor and activist, Fran Visco, impacted and transformed breast cancer research.

A dozen years ago, the V in Fran Visco's name could also have stood for "vilified." Now, it could stand for "victory," "vindicated," and "visionary."

Visco is the Philadelphia lawyer who led an alliance of breast cancer groups in getting vast sums of money – \$1.7B and counting – for a whole new breast cancer research realm run by, of all agencies, the U.S. Army.

When the initial \$210M installment was showered on the Army's program in 1993, Visco and her fledgling National Breast Cancer Coalition were widely considered naïve and even dangerous. Critics, particularly at the National Institutes of Health and the National Cancer Institute, warned that the advocates' coup would politicize the scientific process, duplicate efforts, and produce inferior research. In short, waste taxpayers' money.

That has not happened. While breast cancer is still far from being conquered – this year, it will strike 216,000 more women and kill 40,000 – Visco, 56, is now lauded by scientists, policymakers, and advocates as a brilliant leader. Not only has her organization increased breast cancer research funding – worldwide as well in the United States – it has involved advocates in deciding how the money is spent, fostered innovative research that would have been passed over by traditional funding sources, and speeded clinical trials of promising new drugs.

The best-known example of the impact of all this is Herceptin, the revolutionary breast cancer treatment, approved in 1998, that has brought some women with metastatic cancer back from the brink of death...

Is the world close to achieving the coalition's stated goal of wiping out breast cancer?

Visco can point to the Army's enviable statistics – 24,000 proposals, 3,911 funded, 6,200 journal publications, 4,200 presentations at scientific meetings, and 140 patents or licenses. She can cite researchers performing innovative work on breast cancer vaccines, "biomarkers" for early disease detection, and therapies that, like Herceptin, shoot at precise genetic targets. She can take satisfaction in the growth of the Defense Department's research programs, which now include ovarian and prostate cancer...

But, no, she says, the world is not close.

That is why much of her focus is now back where it started – on women like her. The coalition's website is full of information to help make the hard, complex – and irrevocable – choices that may save, or at least extend, their lives.

program to identify underfunded and underrepresented areas of research and to encourage research in those areas that are considered the most critical to patients, consumers, clinicians, and laboratory researchers. The investment strategy provides the framework and direction necessary to most effectively obligate each congressional appropriation, while avoiding unnecessary duplication with other funding agencies. (See Appendices A and B for summaries of congressional appropriations by program and year.)

# **Program Development and Execution**

A critical component of the investment strategy is developing specific award mechanisms that capture the current needs of both the research and advocacy communities. Separate announcements outlining the award mechanisms offered for each of the research programs managed by the CDMRP are developed in conjunction with each IP and released each FY. The CDMRP has utilized approximately 30 different types of award mechanisms that fall into three categories: research, training and recruitment, and research resources.<sup>4</sup> See Section II for summary tables of many of the different award mechanisms used by the CDMRP.

<sup>&</sup>lt;sup>4</sup> For a summary of many of the award mechanisms offered by the CDMRP between 1993 and 1999, see Appendix A of the DOD CDMRP Annual Report, September 1999.



Figure I-7. CDMRP Flexible Execution and Management Cycle

Proposals received in response to published announcements are subjected to a two-tier review. The CDMRP model for performing these reviews derives from the 1993 IOM recommendations.<sup>5</sup> The two tiers are fundamentally different. The first tier is a scientific peer review of proposals against established criteria for determination of scientific merit. Panels organized by scientific discipline, specialty area, or award mechanism conduct scientific peer review. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of proposals, based upon the review criteria published for each award mechanism. The second tier of the review process is programmatic review. Programmatic review is accomplished by the IP, the advisors that recommend the initial investment strategy. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool against published review criteria. Scientifically sound proposals that most effectively address the unique focus and goals of the program are then recommended to the Commanding General, USAMRMC, for funding.

# **Grants Management**

Awards are made in the form of grants, contracts, or cooperative agreements, and the research is executed over 1 to 5 years, depending on the type of award mechanism. With 5,627 awards made through FY03, the management of these grants, contracts, and/or cooperative agreements is a major focus of the CDMRP. As such, the CDMRP makes certain that the research supported by the American public is monitored thoroughly for technical progress and compliance with animal and human use regulations.

Every CDMRP award is assigned to a Grants Manager for the life of that grant, ensuring a broad knowledge of each grant, continuity among all parties involved in the award, and the most comprehensive assistance possible to the Principal Investigator (PI). The Grants Manager is a doctorate level scientist or clinician and is the primary technical representative for the management of the award. During the pre-award process, the Grants Managers assess overlap with other funding agencies, ensure the completeness of the required regulatory documents, and serve as a liaison between investigators and representatives at the USAMRMC. During the life of the award, Grants Managers monitor the technical progress of the overall grant, facilitate the resolution of changes or issues, and maintain regular communication with each PI.

# **Program Evaluation**

The CDMRP's program evaluation division was established to assess research program operations and outcomes. The impetus for assessing the organization's processes and achievements was multifactorial. First, in late 1995, the USAMRMC commissioned the IOM to review the progress of the BCRP. The IOM was asked to include a review of the portfolio of funded research, assess program management and achievements, and recommend areas for funding that have not been funded or areas that need additional emphasis. The result of this review was a report published in 1997<sup>6</sup> that concluded with 3 major and

<sup>&</sup>lt;sup>5</sup> Institute of Medicine, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, 1993.

<sup>&</sup>lt;sup>6</sup> Institute of Medicine, *A Review of the Department of Defense's Program for Breast Cancer Research.* National Academy Press, Washington DC, 1997.

13 secondary recommendations. One of the major recommendations was that the CDMRP "develop and implement a plan with benchmarks and appropriate tools to measure achievements and progress towards goals of the BCRP both annually and over time." Secondly, the CDMRP is accountable for the expenditure of congressional appropriations – accountable to the consumer advocacy groups, to the scientific community, to Congress, and to the American public at large. Within this context, the CDMRP developed an integrated approach to the evaluation of its programs and processes and established a program evaluation division to specifically assess research relevance, productivity, and accomplishments. Combined with the activities of the grants management division (detailed earlier), these efforts have collectively enabled the CDMRP to evaluate program operations and outcomes. The following list highlights some of the efforts of the program evaluation division:

■ The development and launch of an on-line survey for CDMRP grant applicants and recipients to assess the level of satisfaction with the CDMRP application, funding, and grant management procedures and the extent to which these CDMRP customers believe the CDMRP has achieved its program goals. Findings indicate that the majority of grant applicants surveyed are clear about and satisfied with the CDMRP review process, review criteria, and funding decision their application received. Areas that reflect the need for further enhancement or clarity, such as regulatory requirements for funded awards, are being evaluated to ease applicants' navigation through various CDMRP operations.

■ The development of a new electronic

the entire CDMRP research portfolio. This innovative system will identify outcomes of CDMRP research and verify our return on investment. Currently under development, the system will be used to catalog and track research advances attributed to CDMRP investigators as well as allow our staff to better assist researchers with their grants and clinical protocols. Ultimately, such improvements in grants and information management will lead to further advances in disease prevention, treatment, and management.

■ The development and launch of a survey to assess the degree to which the BCRP training awards have been successful in attracting and keeping new and productive investigators in the field of breast cancer research, thereby quickening the pace of breast cancer research. Preliminary findings from trainees surveyed indicate that BCRP training awards have been largely successful in attracting and retaining new investigators into the field of breast cancer research. The majority of trainees have remained in the field, and over half are involved in some aspect of research. However, most of the trainees are still very early in their careers, or in training, and the true impact of their presence in this area will not be known for many years.

### **Research Information Dissemination**

The CDMRP recognizes the importance of disseminating program information to the public and has supported several efforts to foster program awareness.

# http://cdmrp.army.mil

research community; today, approximately 150,000 visits are made annually to the CDMRP home page along with over 500,000 total visits to the overall website annually. Features of the

The CDMRP website disseminates up-to-date

- Research Programs individual programs managed by the CDMRP
- Research Highlights scientific accomplishments achieved by CDMRP-funded investigators
- Funding Opportunities calls to the scientific and clinical communities to submit proposals
- CDMRP Annual Reports archived CDMRP Annual Reports
- Search Awards search engines for posted awards that search by various criteria (including research program, FY, PI, institution, research topic, award mechanism, and clinical trial); award amounts, abstracts, and publications are provided for each award
- Consumer Involvement information on consumer involvement in scientific peer review
- Publications documents such as press releases, fact sheets, peer reviewed articles, and program award books
- Resources & Links links to other sites
  Recently, an evaluation of the CDMRP website was
  conducted to measure user effectiveness, efficiency,
  and satisfaction. Findings from this evaluation will
  be used to improve the website so that users will
  be able to continue to effectively and efficiently
  navigate the site.

# Advertisement of Funding Opportunities and Award Information

Programs within the CDMRP prepare and issue Program Announcements that provide details on individual award mechanisms, the application process, and requirements for submitting proposals. Once proposals have been funded, the CDMRP promotes public awareness of funded awards. The following publicity efforts are directed toward alerting the scientific research community when new Program Announcements are released and propagating the word on funded awards:

- Posting the Program Announcements on the CDMRP website to enable immediate access
- Alerting over 600 Research Administrators of upcoming award opportunities with preannouncements and release date announcements

- Notifying over 50 professional associations (e.g., the American Association of Cancer Research [AACR] and the American Society of Clinical Oncology), 10 military research laboratories, 6 federal agencies, and over 150 consumer advocacy organizations of upcoming funding opportunities
- Advertising in both broadly focused professional journals (e.g., Science) and federal business websites (e.g., FedBizOpps)
- Targeted e-mails and advertising (e.g., *New York Times* and *Wall Street Journal*) for mechanisms that are aimed toward recruiting new applicants or scientists in specific research areas
- Sending e-mails to prior applicants, scientific peer reviewers, and individuals who have requested that their names be placed on the CDMRP mailing list
- Sending press releases to cancer research news outlets such as The Scientist, Oncology Times, BioWorld, Eureka, Yahoo, and Science Daily Magazine
- Notifying websites that specialize in biomedical grant notification, including Community of Science, Science: Grants Net, and ASTRO Awards Monitor
- Exhibiting the CDMRP displays at national scientific meetings such as the AACR, American Society of Clinical Oncology, and the American Urological Association; at military conferences such as the Association of the United States Army; and at minority research institutions and various symposiums including the Hispanic Association of Colleges & Universities, Weekend of Hope, and Neurofibromatosis Symposium
- Distributing over 600 electronic news items, including congressional appropriations, upcoming funding opportunities, research highlights, and the CDMRP Annual Report to over 150 consumer advocacy groups, including the National Breast Cancer Coalition; US TOO International, Inc.; and National Neurofibromatosis Foundation, Inc.
- Immediately posting award information on the CDMRP website and encouraging recipient institutions to use both internal and external communications to do the same
- Initiating a planned placement campaign to announce FYO3 PCRP awards

- Sponsoring accomplished PCRP awardees to attend and present their CDMRP research achievements at the Annual Scientific Retreats held by the nonprofit, public charity, the Prostate Cancer Foundation, formerly known as CaP CURE (the Association for the Cure of Cancer of the Prostate); since 2001, 19 PCRP awardees have attended the retreats
- Sponsoring PRMRP FY99–02 award recipients to present their CDMRP research achievements at the first Military Health Research Forum held in San Juan, Puerto Rico (see related box story on page VII-6 for additional information about this meeting)

### **Publications**

Over 6,000 publications have resulted from investigators who received CDMRP awards through FY02. Citations for these publications are provided to the CDMRP by award recipients. In addition, the CDMRP staff has published articles and presented information at national scientific meetings. A list of the recent CDMRP peer reviewed articles, abstracts, and posters can be found on the CDMRP website at http://cdmrp.army.mil/pubs.

# COL Kenneth Bertram —"It's our job to put ourselves out of business."

Adapted from "DoD Funds Overlooked Cancer Research Area" by Sandra Basu, U.S. Medicine August 2004 FORT DETRICK, MD.—Unlike most people, COL Kenneth Bertram, MC, USA, is looking forward to the day that his job disappears. It is not that Dr. Bertram dislikes his job as the director of the Department of Defense's Congressionally Directed Medical Research Programs (CDMRP), which oversees the Breast Cancer Research Program (BCRP), but he is hopeful that one day breast cancer will be eradicated and there will no longer be a need for the program.

"It's our job to put ourselves out of business. Hopefully, we will play a part in whatever the breakthrough is to eradicate cancer and then I'm looking forward to a very big party and then we can go and attack something else," said Dr. Bertram.

Until that day comes, Dr. Bertram remains busy overseeing the program, which is now in its 12th year and is the second largest funder of extramural breast cancer research in the world after the National Institutes of Health (NIH)...

Dr. Bertram, an oncologist, explains that the program is unique because it looks to fund high-risk projects, such as new ideas about treating and eradicating breast cancer that have not been tested before. Breast cancer projects that take research in a new direction or go against mainstream scientific thought might have difficulty finding funding. The BCRP has the mission of funding promising ideas that fall in this category. The expectation is that by exploring new areas, progress will be made in making a discovery...

"The hallmark of the program is to look for areas of underfunding, to be willing to take risks. The person who comes in with an idea that flows against mainstream science, we are willing to fund that, because if it works we are going to have a tremendous leap forward in understanding breast cancer or a potential or realized drug," Dr. Bertram said...

This entire feature article can be accessed at http://www.usmedicine.com/article.cfm?articleID=921&issueID=65.

I-10 Overview of the CDMRP